REMARKS

Claims 1, 18 and 22 have been amended. Claims 1-15 and 18-22 remain for consideration. No new matter has been added.

The objections and the rejections shall be taken up in the order presented in the Official Action (hereinafter "Action").

6. Claims 1, 2 and 4-10 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 6,469,785 to Duveneck et al. (hereinafter "Duveneck") in view of U.S. Patent No. 4,621,059 to Rokugawa (hereinafter "Rokugawa").

CLAIM 1

Amended claim 1 recites a device for detecting a cellular metabolic process associated with a cell by detecting a luminescence event in, at, or in the immediate vicinity of the cell. The device includes:

> "a carrier element with a surface prepared for coupling of the cell thereto;
> a detector for receiving a luminescence signal indicative of the luminescent event **through the prepared surface**, where the detector is integrated into the carrier element below the prepared surface;
> a cover covering the prepared surface to form a cavity, the cover having an inlet and an outlet; and
> a metabolically-influencing cell excitation reservoir connected to the inlet and containing a biological or chemical excitation medium that includes a luminophore, where the excitation medium influences the metabolism of the cell during excitation thereof by the medium, and **where the luminophore reacts with a metabolic product of the cell during the excitation thereof to thereby provide the luminescence signal**." (Emphasis added).

The Action contends that the combination of Duveneck and Rokugawa teaches such a device. Specifically, the Action contends that the optical detection device disclosed in Duveneck is capable of performing "applicant's stated intended use." (Action, pg 6). In addition, the Action

contends that Duveneck discloses a detector for receiving a luminescence signal. (Action, pg 5). Applicants respectfully disagree.

THE OPTICAL DETECTION DEVICE IN DUVENECK IS INCOMPATIBLE WITH THE FEATURE OF A METABOLICALLY-INFLUENCING CELL EXCITATION RESERVOIR...

Applicants respectfully submit that the optical detection device disclosed in Duveneck is incompatible with the claimed feature of "*a metabolically-influencing cell excitation reservoir connected to the inlet and containing a biological or chemical excitation medium that includes a luminophore, where the excitation medium influences the metabolism of the cell during excitation thereof by the medium, and* ***where the luminophore reacts with a metabolic product of the cell during the excitation thereof to thereby provide the luminescence signal***." That is, if the inlet channel 64 in Duveneck (see FIG. 1) was connected to a reservoir capable of being used as a metabolically-influencing cell excitation reservoir as suggested in the Action (see pg 6), then the device of Duveneck would no longer be operable for its intended purpose. Specifically, Duveneck teaches the use of an optical excitation source (i.e., a semiconductor laser 10). Modifying Duveneck to receive a biological or chemical excitation medium from a reservoir (or source) would change the detection principle of Duveneck, which relies upon the semiconductor laser 10 to radiate excitation light, and not the reaction of a luminophore with a metabolic product of the cell during the excitation thereof to thereby provide the luminescence signal.

In contrast to claim 1, Duveneck teaches, as illustrated in FIG. 1, that "[leading] into the measuring chamber 68 are an inlet channel 64 and an outlet channel 66 through which the fluid samples to be examined can be circulated through the measuring chamber 68 and past the sensor layer 8." (Duveneck, col. 7, lines 5-8). With regards to the measurement of analytes within the fluid sample, Duveneck teaches the following:

> "The measuring method of the device... relies on the interaction of the evanescent light intensity with the sensor layer 8. The actual measurement can be carried out by radiating in the excitation light continuously, in continuous-wave (cw) operation, that is to say preferably with excitation at a light intensity that is constant with time. Alternatively, however, the measurement can be carried out by radiating in the excitation light in the form of timed pulses... with which the luminescence can be detected in a time-resolved manner...." (col. 7, lines 56-67).

Thus, according to a fair and proper reading of Duveneck, optical excitation of the luminescent radiation occurs via the evanescent field within the waveguide 6. (Duveneck, col. 7, line 5-14 and 56-67). That is, the luminescent radiation is NOT excited chemically or biologically, but instead excited optically by excitation radiation 70 created by a semiconductor laser 10 and coupled into an optical waveguide 6.

Due to the foregoing, even assuming, without admitting, that Duveneck and Rokugawa are properly combinable, a person of ordinary skill in the art would still not use the reservoir in such a combination as the recited metabolically-influencing cell excitation reservoir. Specifically, Duveneck teaches exciting the sample to be measured (i.e., the analyte) using an evanescent field via the semiconductor laser 10, whereas claim 1 recites that a luminophore from a biological or chemical excitation medium contained in the metabolically-influencing cell excitation reservoir "reacts with a metabolic product of the cell during the excitation thereof to thereby provide the luminescence signal." Duveneck further teaches an optical excitation of the luminescent radiation via the evanescent field within the waveguide. However, the evanescent field appears just in direct ambience to the bounding surface of the waveguide. With accretive distance to the bounding surface, the intensity of the evanescent field is reduced exponentially.

Because of the much bigger dimensions of biological cells than the thickness of the layer in which the evanescent field is present (about 200 nm), a person skilled in the art would not consider docking a biological cell on the interface of the waveguide, in order to analyze it with

the evanescent radiation. The evanescent radiation would not even or not sufficiently break into the cell.

As a result, there would be no reasonable expectation of success by using both light sources (i.e., the substrate laser 10 of Duveneck and the luminescent event recited in claim 1), since the luminescence signal would add an additional complex variable that would have to be accounted for by the light detector in Duveneck. For example, the light detector may not be able to distinguish between light emitted from and the intensity of the substrate laser 10 versus luminescence signal from the luminescent event, and therefore could not properly measure sample characteristics. Therefore, applicants respectfully submit that a person of ordinary skill in the art would NOT have been motivated to use the reservoir in the alleged combination of Duveneck and Rokugawa as the recited "metabolically-influencing cell excitation reservoir...."

THE ALLEGED COMBINATION OF DUVENECK AND ROKUGAWA FAILS TO TEACH OR SUGGEST THE FEATURE OF A DETECTOR...

The Action contends that the recited "*carrier element...*" and "*detector for receiving a luminescence signal...*" reads on the carrier 76, the substrate 7 and the photoelectronic detection unit 4 disclosed in Duveneck. Applicants respectfully submit that these contentions are now moot since claim 1 has been amended. Specifically, as amended, the detector receives "*a luminescence signal indicative of the luminescent event through the prepared surface*" of the carrier element, where the surface is prepared for coupling of a cell thereto. In contrast, Duveneck teaches, as illustrated in FIG. 1, that radiation 70 emitted from the surface-emitting semiconductor laser 10 is directed into the waveguide 6 via a grating 61 in the substrate 7 and a coupling-in grating 60 in the intermediate layer 9. (Col. 7, lines 44-52). The radiation 72 travels through the waveguide 6 and is directed to the photoelectric detection unit 4 via a coupling-out

grating 62 in the intermediate layer 9 and a grating 63 in the substrate 7. (Col. 7, lines 44-52; FIG. 1). Notably, Duveneck fails to teach or suggest that any of these gratings 60-63 have a surface prepared for coupling a cell thereto. Therefore, the alleged combination of Duveneck and Rokugawa would merely teach directing radiation through the gratings 60-63 and not through a prepared surface. For at least the foregoing reasons, applicants respectfully submit that claim 1 is patentable over the alleged combination of Duveneck and Rokugawa.

CLAIMS 2 AND 4-10

Applicants respectfully submit that these rejections are moot since claim 1 is patentable for at least the reasons as set forth above.

7. Claim 3 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa and U.S. Patent No. 6,104,495 to Sieben et al. (hereinafter "Sieben").

Applicants respectfully submit that this rejection is moot since claim 1 is patentable for at least the reasons as set forth above.

8. Claims 12 and 14 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa and PCT Application No. WO 2001/043875 to Schurmann-Mader et al. (hereinafter "Mader").

Applicants respectfully submit that these rejections are moot since claim 1 is patentable for at least the reasons as set forth above.

9. Claims 11 and 15 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa and U.S. Patent No. 5,278,048 to Parce et al. (hereinafter "Parce").

Applicants respectfully submit that these rejections are moot since claim 1 is patentable for at least the reasons as set forth above.

10. Claim 13 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa, Mader and U.S. Patent No. 5,582,697 to Ikeda et al. (hereinafter "Ikeda").

Applicants respectfully submit that this rejection is moot since claim 1 is patentable for at least the reasons as set forth above.

11. Claims 18, 19 and 22 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view Rokugawa and Sieben.

CLAIM 18

Amended claim 18 recites a device for detecting a cellular metabolic process associated with a cell by detecting a luminescence event in, at, or in the immediate vicinity of the cell. As amended, the device includes:

> "a semiconductive device with a surface prepared for coupling of the cell thereto;
>
> a detector for receiving a luminescence signal indicative of the luminescent event **through the prepared surface**, where the detector is integrated into the semiconductive device below the cell;
>
> a cover that covers the prepared surface to form a cavity, the cover having an inlet and an outlet; and
>
> a metabolically-influencing cell excitation reservoir that provides to the cavity via the inlet a biological or chemical excitation medium that includes a

> luminophore, where the excitation medium influences the metabolism of the cell during excitation thereof by the medium, and **where the luminophore reacts with a metabolic product of the cell during the excitation thereof to provide luminescence detected by the detector**." (Emphasis added).

The Action contends that the combination of Duveneck, Rokugawa and Sieben teaches such a device. Specifically, the Action contends that the optical detection device disclosed in Duveneck is capable of performing "applicant's stated intended use." (Action, pgs, 6 and 14-15). In addition, the Action contends that the recited "surface prepared for coupling of the cell thereto..." and "detector for receiving a luminescence signal..." reads on the carrier 76, the substrate 7 and the photoelectronic detection unit 4 disclosed in Duveneck. (Action, pg 13). Applicants respectfully disagree and submit that claim 18 is patentable for at least similar reasons as set forth above with respect to claim 1.

CLAIM 19

Applicants respectfully submit that this rejection is moot since claim 18 is patentable for at least the reasons as set forth above.

CLAIM 22

Amended claim 22 recites a device for detecting a cellular metabolic process associated with a cell by detecting a luminescence event. As amended, the device includes:

> "a semiconductive device with a surface prepared with a cell-immobilizing medium for coupling and immobilizing of the cell thereto;
>
> a detector for receiving a luminescence signal indicative of the luminescent event **through the prepared surface**, where the detector is integrated into the semiconductive device below the cell and prepared surface;
>
> a housing that in cooperation with the prepared surface forms a cavity having an inlet and an outlet; and
>
> one of a metabolically-influencing cell excitation reservoir that provides to the cavity via the inlet a biological or chemical excitation medium that includes a luminophore, where the excitation medium influences the metabolism of the cell

and **the luminophore reacts with a metabolic product of the cell to provide luminescence detected by the detector**." (Emphasis added).

The Action contends that the combination of Duveneck, Rokugawa and Sieben teaches such a device. Specifically, the Action contends that the optical detection device disclosed in Duveneck is capable of performing "applicant's stated intended use." (Action, pgs 6 and 14-15). In addition, the Action contends that the claimed features "*surface prepared with a cell-immobilizing medium for coupling and immobilizing of the cell thereto...*" and "*detector for receiving a luminescence signal...*" reads on the carrier 76, the substrate 7 and the photoelectronic detection unit 4 disclosed in Duveneck. (Action, pg 13). Applicants respectfully disagree and submit that claim 22 is patentable for at least similar reasons as set forth above with respect to claim 1.

12. Claim 20 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view Sieben and Rokugawa.

Applicants respectfully submit that this rejection is moot since claim 18 is patentable for at least the reasons as set forth above.

13. Claim 21 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view Sieben and Mader.

Applicants respectfully submit that this rejection is moot since claim 18 is patentable for at least the reasons as set forth above.

For all the foregoing reasons, reconsideration and allowance of claims 1-15 and 18-22 is respectfully requested.

If a telephone interview could assist in the prosecution of this application, please call the undersigned attorney.

Respectfully submitted,

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